

Claims

1. A process for the solid phase synthesis of bio-oligomers characterised in that at least one washing step is carried out in the presence of a salt $(X^{n+})_m(Y^{m-})_n$, wherein X represents a cation, n represents the charge of the cation, y represents an anion and m represents the charge of the anion.
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2. A process for attaching an appropriately protected monomer or oligomer to another monomer or oligomer which is protected by a protecting group and which is attached to a support, comprising the following steps:
 - a) cleave the protecting group from the monomer or oligomer attached to the support; and then
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 - b) perform a thorough washing; and then
 - c) add an appropriately protected monomer or oligomer and couple it to the monomer or oligomer that is attached to the support, to form a covalent bond; characterized in that during the process, a salt $(X^{n+})_m(Y^{m-})_n$ which is soluble in a solvent used in this process, is added, wherein, if the salt $(X^{n+})_m(Y^{m-})_n$ is added in step
15 c), the solvent is neither a chloroform/phenol nor a chloroform/trifluoroethanol mixture.
3. A process for attaching an α -amino protected amino acid or peptide having an unprotected C-terminus to another amino acid or peptide which is protected by an α -amino protecting group and which is attached to a support during solid phase peptide synthesis comprising the following steps:
 - a) cleave the α -amino protecting group from the amino acid or peptide attached to the support; and then
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 - b) perform a thorough washing; and then
 - c) add an α -amino protected amino acid or peptide having an unprotected C-terminus and couple it to the amino acid or peptide that is attached to the support and that now has an unprotected N-terminus, to form an amide bond; characterized in that during the process, a salt $(X^{n+})_m(Y^{m-})_n$, which is soluble in a solvent used in this process, is added, wherein, if the salt $(X^{n+})_m(Y^{m-})_n$ is added in step
25 c), the solvent is neither a chloroform/phenol nor a chloroform/trifluoroethanol mixture.
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4. A process according to claim 2 or 3, which additionally comprises the following step:
 - d) perform a thorough washing;
wherein step d) is performed after step c).

5. A process for attaching an α -amino protected amino acid or peptide having an unprotected C-terminus to another amino acid or peptide which is protected by an α -amino protecting group and which is attached to a support during solid phase peptide synthesis comprising the following steps:
- 5 a) cleave the α -amino protecting group from the amino acid or peptide attached to the support;
- b) perform a thorough washing;
- c) add an α -amino protected amino acid or peptide having an unprotected C-terminus and couple it to the amino acid or peptide that is attached to the support
- 10 and that now has an unprotected N-terminus, to form an amide bond; and
- d) perform another thorough washing;
- characterized in that at least in step a), a salt $(X^{n+})_m(Y^{m-})_n$, which is soluble in a solvent used in this step, is added.
6. A process for attaching an α -amino protected amino acid or peptide having an
- 15 unprotected C-terminus to another amino acid or peptide which is protected by an α -amino protecting group and which is attached to a support during solid phase peptide synthesis comprising the following steps:
- a) cleave the α -amino protecting group from the amino acid or peptide attached to the support;
- 20 b) perform a thorough washing;
- c) add an α -amino protected amino acid or peptide having an unprotected C-terminus and couple it to the amino acid or peptide that is attached to the support and that now has an unprotected N-terminus, to form an amide bond;
- d) perform another thorough washing; and
- 25 characterized in that at least in step b), a salt $(X^{n+})_m(Y^{m-})_n$, which is soluble in a solvent used in this step, is added.
7. A process for attaching an α -amino protected amino acid or peptide having an
- unprotected C-terminus to another amino acid or peptide which is protected by an α -amino protecting group and which is attached to a support during solid phase peptide
- 30 synthesis comprising the following steps:
- a) cleave the α -amino protecting group from the amino acid or peptide attached to the support;
- b) perform a thorough washing;

- c) add an α -amino protected amino acid or peptide having an unprotected C-terminus and couple it to the amino acid or peptide that is attached to the support and that now has an unprotected N-terminus, to form an amide bond; and
d) perform another thorough washing;
- 5 characterized in that at least in step c), a salt $(X^{n+})_m(Y^{m-})_n$, which is soluble in a solvent used in this step, is added, wherein the solvent is neither a chloroform/phenol nor a chloroform/trifluoroethanol mixture.
8. A process for attaching an α -amino protected amino acid or peptide having an unprotected C-terminus to another amino acid or peptide which is protected by an α -amino protecting group and which is attached to a support during solid phase peptide synthesis comprising the following steps:
- 10 a) cleave the α -amino protecting group from the amino acid or peptide attached to the support;
b) perform a thorough washing;
- 15 c) add an α -amino protected amino acid or peptide having an unprotected C-terminus and couple it to the amino acid or peptide that is attached to the support and that now has an unprotected N-terminus, to form an amide bond; and
d) perform another thorough washing;
- 20 characterized in that at least in step d), a salt $(X^{n+})_m(Y^{m-})_n$, which is soluble in a solvent used in this step, is added.
9. A process according to any of claims 1 to 8 wherein the salt $(X^{n+})_m(Y^{m-})_n$ is selected from the group of quaternary ammonium salts, ionic liquids, phosphonium salts, sulfonium salts, inorganic salts or any mixture thereof.
- 25 10. A process according to claim 9 wherein $(Y^{m-})_n$ is selected from the group of fluoride, chloride, bromide, iodide, hydroxide, carbonate, hydrogenocarbonate, nitrate, phosphate, hydrogenophosphate, dihydrogenophosphate, tetrafluoroborate, hexafluorophosphate, acetate, carboxylates, cyanides, isocyanates, tetra-alkylborates, tetra-arylborates, trifluoroacetate, tosylate, mesylate or any mixture thereof.
- 30 11. A process according to claim 9 wherein the quaternary ammonium salt is selected from benzyltrimethylammonium hydroxide, benzyltrimethylammonium chloride or benzyltrimethylammonium carbonate, the phosphonium salt is tetrabutylphosphonium bromide and the sulfonium salt is triethylsulfonium tetrafluoroborate.

12. A process according to any of claims 2 to 11 wherein the salt added in step a), b), c) or d) is also added in one or more of the other steps.
13. A process according to any of claims 3 to 12 wherein the α -amino protecting group is Fmoc (9-fluorenylmethoxycarbonyl) or Nsc (p-Nitrophenylsulphonylethoxycarbonate) or any other base-cleavable protecting group.
14. A process according to any of claims 3 to 12 wherein the α -amino protecting group is Boc (tert-butoxycarbonyl), Trt (trityl), Bpoc (2-p-Biphenylisopropylloxycarbonyl) or any other acid-cleavable protecting group.
15. A process according to any of claims 3 to 12 wherein the α -amino protecting group is selected so that neither acid nor base treatment is required for its cleavage.
16. A process for synthesising a peptide comprising:
- a') attaching a first amino acid or peptide, having an α -amino protecting group, via its C-terminus to a functionalized support;
 - b') perform the process according to any of claims 3 to 15 with the following amino acid or peptide foreseen in the sequence;
 - c') repeat step b' with the appropriate amino acids or peptides until the desired sequence is achieved; and
 - d') cleave the assembled peptide from the support by an appropriate method.
17. Use of a salt $(X^{n+})_m(Y^{m-})_n$ in solid phase peptide synthesis for improving the washing of the peptide resin.
18. Use according to claim 17 for improving the elimination of excess amino acids or cleavage reagents.